

Office Action Summary	Application No. 10/581,228	Applicant(s) CHIORINI ET AL.
	Examiner MICHAEL BURKHART	Art Unit 1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 May 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 112-152 is/are pending in the application.
- 4a) Of the above claim(s) 141-144 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 112-118, 120, 122, 126-140, and 145-151 is/are rejected.
- 7) ☒ Claim(s) 119, 121, 123-125 and 152 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>4/28/11</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt and entry of the amendment dated 5/12/2011 is acknowledged.

Election/Restrictions

Due to amendment of claim 112, claims 122, 123 and 125 are rejoined. Claims 141-144 have not been rejoined and remain drawn to non-elected subject matter for reasons of record. The independent claim (131) requires "two vectors" (line 1), and there is no limitation requiring the "a second vector" as found in line 9 be vector number two of the claim. It is suggested applicants amend the claim such that the "second vector" is the second of the two vectors recited in line 1.

Claim Objections

Claims 131 and 151 are objected to because of the following informalities: the claims recite non-elected subject matter, i.e. in part (c) in claim 151. As currently worded, the claims do not require either of the elected components of the invention, i.e. parts (a) and (b), or part (a) in claim 131. If applicants would like to include the subject matter of claim 151, part (c), the scope of claim 145 is suggested, i.e. the use of the conjunction "and" to link the required components and removal of the Markush language in lines 2-3. Appropriate correction is required.

Claim 122 is objected to because of the following informalities: "at lest" in line 2 should be "at least." Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 151 is rejected under 35 U.S.C. 102(e) as being anticipated by Arbetman et al (US 7,259,151, e.f.d. 6/19/2003, of record).

Arbetman et al disclose a protein (SEQ ID NO: 26) and nucleic acid encoding the protein (SEQ ID NO: 25). SEQ ID NO: 26 of Arbetman et al is 99% identical to instant SEQ ID NO: 7. Applicants alignment provided on page 11 (exhibit C) does not appear to represent SEQ ID NO: 26 of Arbetman et al, as several residues are incorrect in the alignment. As a limited example SEQ ID NO: 26 does include a G at residue 17, but does not in applicants alignment, and includes an M at residue 193, but does not in applicants alignment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 112-118, 120,122, 126-140, and 145-151 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising the BAAV ITR and capsid protein set forth in SEQ ID NOs: 12 and 10, respectively, does not

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reasonably provide enablement for other BAAV ITRs, capsid proteins, or variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claims 112-118, 120, 122, 126-140, and 145-151 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Response to Arguments

Applicant's arguments filed 5/12/2011 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) the reasons set forth by the Examiner for rejecting the claims for lack of enablement are nearly identical to those in *Ex Parte Kubin*, wherein the Examiner was reversed; 2) the Written Description Examples in the USPTO guidelines indicate that the written description requirement has been met in the instant case.

Regarding both 1) and 2), To put the situation in perspective, the number of possible amino acid sequences of 538 amino acids in length (SEQ ID NO: 11 is 538) is 20^{500} (approx. 10^{650}). The number of possible nucleotide or amino acid sequences that are of a given % identity relative to a reference sequence, where all differences between the possible sequences and the reference sequence are substitutions, can be calculated by the following expansion formula:

$$N = XL + X^2L(L-1)/2! + X^3L(L-1)(L-2)/3! + \dots + X^{n-1}L(L-1)(L-2)\dots(L-(n-2))/(n-1)! + X^nL(L-1)(L-2)\dots(L-(n-1))/n!$$

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where N is the number of possible sequences, X is the number of different residues that can be substituted for a residue in the reference sequence, L is the length of the reference sequence, n is the maximum number of residues that can be substituted relative to the reference sequence at a given % identity. For a nucleotide sequence, X is 3 (alternate nucleotides); for an amino acid sequence, X is 19 (alternate amino acids). The n^{th} term of the expansion can be rewritten as:

$$X^n \cdot \frac{L!}{n! (L-(n-1))!}$$

For a 538 amino acid sequence that is at least 95% identical to a reference sequence of 538 amino acids, e.g. SEQ ID NO: 1, the number of possible sequences having 27 amino acid substitutions relative to the reference) is approximately 2×10^{65} . So the last term is approximately equal to N, i.e. the preceding terms contribute little to the total. Also, as the number of permitted substitutions increases the number of possible variant sequences increases geometrically. In a genus of polypeptides that are at least 95% identical to a reference, nearly all will be exactly 95% identical. While limiting the scope of potential sequences to those that are at least 95 -97% identical to a reference, for example, greatly reduces the number of potential sequences to test, it does not do so in any meaningful way.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL BURKHART whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhardt/
Primary Examiner, Art Unit 1633